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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/545,162	04/07/2000	ANTHONY P. SHUBER	EXT-026	1013

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Patent Administrator  
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EXAMINER

EINSMANN, JULIET CAROLINE

ART UNIT PAPER NUMBER

1634

DATE MAILED: 10/22/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/545,162

Applicant(s)

LAPIDUS ET AL.

Examiner

Juliet C Einsmann

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 7-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 07 April 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: CRF. Problem Report

### DETAILED ACTION

1. This action is written in response applicant's correspondence submitted 4/19/02, paper number 8. Claims 7 and 8 have been amended, claims 2-5 have been canceled, and claims 10-14 have been added. Claims 7-14 are pending. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections not reiterated in this action have been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. **This action is final.**

#### *Specification*

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): The application recites nucleic acid sequences, but there is no CRF on file (see, for example, pages 15 and 16).

In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit a CRF and paper copy of the Sequence Listing containing these sequences, an amendment directing the entry of the Sequence Listing into the specification, and a letter stating that the content of the paper and computer readable copies are the same.

3. Applicant's CRF filed 4/19/02 was not sufficient to overcome these concerns because the CRF was damaged upon receipt at the USPTO. Applicant is required to send in a new CRF, and a letter stating the content of the paper copy filed 4/19/02 and the new CRF are the same, or a new paper copy, as appropriate (see attached CRF Problem Report).

*Claim Rejections - 35 USC § 112*

4. Claims 9-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for screening a patient for colorectal cancer or precancer by determining in fecal matter a ratio between a first amount of long nucleic acid of a length greater than 200 base pairs and a second amount of nucleic acid of a length less than said long nucleic acid, does not reasonably provide enablement for the detection of other types of cancer or precancer or the use of tissues or body fluids other than fecal matter or methods which do not specify the length of the nucleic acids which are detected. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claimed invention is drawn to encompass the identification of patients having any cancer or precancer by determining, in any body fluid or tissue comprising exfoliated cells, the presence of a fragment of nucleic acid that is "of a greater length than a length of said nucleic acid expected to be present in a sample from a healthy person" or whether an amount of DNA fragment greater than 200 base pairs exceeds a predetermined amount, wherein the DNA fragment is a degradation product of DNA that is present in both normal and precancerous cells or the ratio of long nucleic acids versus short nucleic acids. The specification demonstrates the method using a fecal matter sample for the screening of a patient for colorectal cancer or precancer by detecting the amount of three different long nucleic acid molecules (p53, K-ras, and apc). The specification demonstrates that for these three molecules PCR products of longer than 200 base pairs were present in the fecal matter of patients with colorectal cancer or precancer but such fragments were not present in healthy patients (Example 1). Neither the specification nor

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the prior art demonstrate that such a relationship exists for other cancers or for other body fluids or for lengths of less than 200 base pairs (as is encompassed by claim 7). The level of unpredictability for the detection of any disease using a nucleic acid assay is quite high. Since neither the specification nor the prior art provide any evidence of a universal association between a ration of nucleic acids greater than 200 base pairs to nucleic acids shorter than 200 base pairs and every cancer and every body fluid, a practitioner wishing to practice the claimed invention would be required to provide the extensive experimentation necessary to demonstrate such an association. Such experimentation would in itself be inventive.

In light of the lack of guidance in the specification and the prior art, and in light of the high level of unpredictability in the instant subject matter, it is concluded that undue experimentation would be required to practice the instant invention commensurate in scope with the claimed invention.

It is noted that the claims that are present in allowed patent US 6143529 are of very similar scope to the instantly claimed invention. The instant rejection is not intended to call into question the validity of these claims because the claims in the '529 patent were allowed over a declaration.

#### **Response to Remarks**

The prior art rejections are withdrawn in light of the newly added limitations to the claims. The amended claims and the newly added claims are herein rejected under 112 1<sup>st</sup> paragraph as necessitated by applicant's amendments. The previous claims were so broad in scope that they were effectively enabled by the combined teachings of the prior art and the

specification. However, the amendments to claims 7 and 8 necessitated the new grounds of rejection.

Applicant argues that the methods of the claimed invention can be extrapolated to any tissue or body fluid that comprises exfoliated cells or cellular debris, but provides no evidence for this assertion or reasoning to rebut the enablement rejection and support this assertion. An attorney's arguments are not substitute for rejections of record. MPEP 716.01(c) makes clear that "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)." Furthermore, the following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary. The enablement rejection above specifically discusses a number of these factors which support the conclusion that undue experimentation would be necessary to practice the claimed invention commensurate in scope with the claims, including the unpredictability in the nucleic acid detection of disease, the presence of working examples in a single type of cancer and a single sample type, and the lack of guidance in the specification concerning the detection of other types of diseases in other sample types. However, applicant did not address these issues in the remarks, merely set forth that because the specification discusses these embodiments that the scope of the claims is enabled. This is not persuasive for the reasons of record.

*Conclusion*

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
Juliet C Einsmann  
Examiner  
Art Unit 1655 1634

October 10, 2002

  
W. Gary Jones  
Supervisory Patent Examiner  
Technology Center 1600